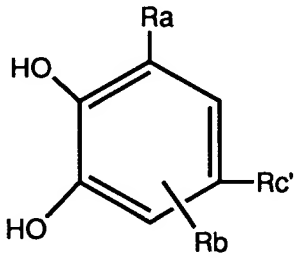
More particularly, claims 8-10 and 16-31 have been withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected species and inventions.

Claims 1-7, 11-15 and 32-39 have been rejected under 35 USC 103 as being unpatentable over Kitahara et al. (USP 4,622,066), British Patent (No. 967,605) or Miyamoto et al., Chem. Abstracts, Vol. 99, 121998j, (1983) for the reasons of record.

It is asserted in the record that the claimed compounds are generically taught by Kitahara et al. and the British patent, and positional isomers are disclosed by Miyamoto et al., and that these disclosures render the claimed compounds prima facie obvious absent a showing of unexpected properties. This rejection is respectfully traversed.

Initially, applications note that the claimed invention comprises a compound of the formula



Ib

wherein Ra is nitro or cyano, Rb is hydrogen or halogen, Rc' is nitro, cyano or the group $-(A)_n-(Q)_m-R^{11}$ or $-(A)_n-Q-R^{21}$, A is vinylene optionally substituted by lower alkyl, n is the integer 0 or 1, m is the integer 0 or 1, R^{11} is the group $-COR^{31}$, an aromatic carbocyclic group, or an aromatic or partially unsaturated heterocyclic group attached via a carbon atom, R^{21} is an optionally substituted, saturated or partially unsaturated lower hydrocarbon residue, R^{31} is hydroxy, amino, an optionally substituted, saturated or partially unsaturated lower

hydrocarbon residue attached via an oxygen atom or an imino or lower alkylimino group or a saturated, N-containing heterocyclic group attached via a ring nitrogen atom, Q is the group -CO- or $>C=N-(Z)p-R^4$, Z is an oxygen atom or an imino group, p is the integer 0 or 1 and R^4 is hydrogen or a saturated or partially unsaturated lower hydrocarbon residue which is optionally substituted and which is optionally attached via a carbonyl group, whereby Ra is cyano when Rc' is cyano or nitro and R^{31} has a significance different from hydroxy when m is the integer 0,

or an ester or ether derivative thereof which is hydrolyzable under physiological conditions or a pharmaceutically acceptable salt thereof.

As is evident, an essential feature of the claimed compounds is the specific substitution pattern. The claimed compounds are benzene derivatives substituted with two hydroxy groups at the 1- and 2-positions, with a nitro or cyano group in the 3-position and with the group Rc' in the 5-position. This very specific substitution pattern is not taught, anticipated or suggested by the cited prior art.

Applicants respectfully submit that it can not be fairly said that one of ordinary skill in this art, through a reading of each of the references, would be in constructive possession of the compounds, that is, compounds generically taught or as positional isomers by the references and alleged to be encompassed by the rejected claims, as opposed to possessing mere language which through tedious extrapolation embraces the names of the claimed compounds. Only with the benefit of hindsight is it possible to interpret the disclosure of the cited references in a fashion to assert a teaching of alleged pertinence to the claimed invention.

With respect to Kitahara, see column 1, lines 26-53, whereby to arrive at a compound which assertedly may be embraced by the recitation in Kitahara, one must go through seven provisos in order to

arrive at a single compound within the wording of the present claims. For example, if one selects R^1 to be the group -OH, m to be 2, the first R^1 to be attached to the 3 position of the benzene ring with respect to the 2-(trifluoromethyl)benzoyl group, the second R^1 to be attached to the 4-position, R^2 to be nitro and to be attached to the 5-position, and n to be 1, then one would, from this speculative reconstruction, with the aid of applicants' disclosure, come up with a compound of formula I wherein Ra is nitro, Rb is hydrogen and Rc' is 2-(trifluoromethyl)benzoyl. Only applicants' disclosure, however, provides the means for the constructive possession of applicants' invention from the language of the reference. It must also be noted that the Kitahara et al. reference does not disclose a single species within applicants' generic formula since nowhere does it teach dihydroxy substitution in any disclosed species, a clear characteristic of the claimed compounds. Significantly also, the reference relates to compounds which are stated to have selective herbicidal activity on grasses and not crops, whereas the claimed compounds are useful in the treatment of, for example, depression and parkinsonism. It is only at column 3, lines 31-33 that Kitahara refers to the use of the compounds as a medicament. In particular, Kitahara provides:

> [t]he fluorine-containing benzophenone derivative (I) according to the present invention is useful not only as a herbicide but also as a medicine or an agricultural chemical such as a plant growth regulator, a germicide, an anti-inflammatory drug, etc.

At best Kitahara represents no more than an invitation to experiment. While Kitahara teaches how to use the compounds disclosed therein as herbicides, Kitahara does not teach how to make or use pharmaceutical compositions containing the benzophenone derivatives. Indeed then, the reference fails to provide a disclosure of compounds which would motivate one of ordinary skill in the art to prepare the claimed compounds and, therefore, fails to suggest the claimed invention.

Those skilled in the art searching for compounds having valuable catechol-O-methyltransferase inhibiting activity would not consult the cited pieces of prior art to develop the claimed compounds. However, even if they did, they would not find any guidance which would lead them to the claimed compounds.

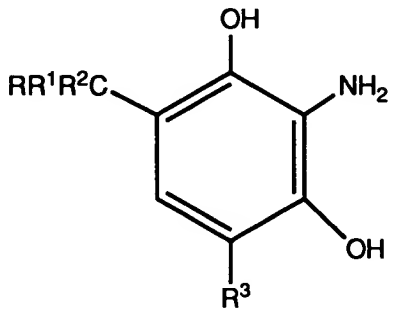
With respect to the cited British patent, it is asserted in the record that said patent allows R' to be hydrogen or halogen, R" to be nitro and benzoyl and n to be the integer 2. Applicants again respectfully submit said reference also represents no more than an invitation to experiment.

More specifically, the British patent relates to a process for the production of orthodihydroxybenzene derivatives. No utility for the myriad of potential derivatives is provided. Furthermore, it does not appear that any species disclosed in the reference reads upon applicants' disclosure. Indeed, the reference then represents no more than a teaching of a process for cleaving of alkyl 0-hydroxyphenyl ethers in the presence of a tertiaryamine and aluminum chloride. Much of the teaching of the reference relates to speculative compounds which could be prepared by the disclosed process. No utility is disclosed for any compounds. Indeed then, the reference provides no motivation to prepare compounds such as those disclosed by applicants and, therefore, fails to support the claimed invention.

It is worth repeating that it can not be fairly and reasonably said that one of ordinary skill in this art through a reading of this entire reference would have constructive possession, or a suggestion of constructive possession, of the compounds which applicants' now claim as opposed to mere language which potentially may embrace the names of some of those compounds. It is only after a review of applicants comprehensive disclosure that one can begin tediously and by the implementation of significant numbers of provisos come

up with one or more species within applicants' disclosure. Such teaching is insufficient to suggest or render obvious the claimed invention.

Finally, with respect to Miyamoto, et al., Miyamoto discloses that compounds of the formula



I

wherein R is alkyl, (un)substituted phenyl, aralkyl; R' is hydrogen, R^2 is hydroxy, alkoxy; R^1 R^2 is 0, inhibit 5-lipoxygenase.

Applicants respectfully submit that the compounds of formula I of Miyamoto differ from the claimed compounds of the invention. The Miyamoto compounds of formula I do not have the specific substitution pattern of the claimed compounds and significantly do not have a nitro or cyano substitutent. At best, Miyamoto, discloses intermediates which are arguendo "positional isomers" of the claimed compounds. Miyamoto does not hint at or suggest the use of these alleged "positional isomers" in pharmaceutical compositions. Miyamoto provides no motivation for using these intermediates as pharmacologically active agents. Significantly, also the compounds of formula I disclosed in Miyamoto et al. are stated to be capable of inhibiting 5-lipoxygenese activity and, thus, have properties which are not comparable to those of the present compounds.

Manifestly, Miyamoto et al. also fails to teach or suggest compounds which would render obvious the claimed invention.

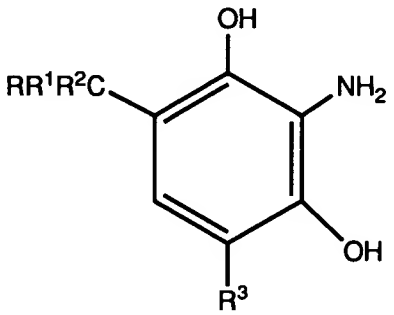
Applicants respectfully submit that the disclosures of the cited references fail to place the claimed invention in the position of the public with the sufficiency required under the Patent Laws and, furthermore, fail to suggest or render obvious the claimed invention. Without the knowledge provided by the claimed invention, those skilled in the art would not be in possession of the compounds alleged to be taught by the cited references.

Accordingly, applicants request that the rejection be withdrawn.

Claims 1 to 7, 11 to 15, and 32 to 39 are rejected under 35 USC 103 as allegedly unpatentable over Watsuka, EP 79141. This rejection is respectfully traversed.

In the Office Action it is asserted that "positional isomers of the instant compounds are taught on page 13, formula III of Watsuka which renders the instant compounds and compositions prima facie obvious absent a showing of unexpected properties."

Watsuka et al., EP 79141, is the publication referred to in Miyamoto. As discussed above, Watsuka discloses compounds of the formula



I

wherein R is alkyl, (un)substituted phenyl, aralkyl, R^1 is hydrogen, R^2 is hydroxy, alkoxy, R^1 R^2 is O, and the use of said compounds for

treating bronchial or lung and tracheal allergic diseases and inflammations induced by prostaglandins. As discussed above, the compounds of formula I do not have the specific substitution pattern of the claimed compounds and more importantly, do not have a nitro or cyano substituent. At best, Watsuka discloses intermediates which arguendo are "positional isomers" of the claimed compound. However, Watsuka provides no motivation for using these intermediates as pharmacologically active agents.

In determining that the board failed to establish prima facie obviousness of an intermediate in view of prior art compounds, the CCPA stated in In re Gyurik and Kingsbury, 201 U.S.P.Q. 552 (CCPA 1979):

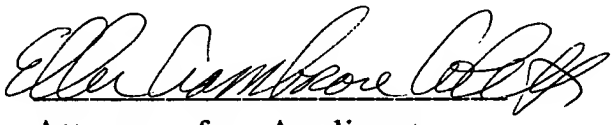
> [a] fundamental principle applicable in assessing the obviousness of chemical compounds is that a compound and its properties are, in patent law, inseparable. In re Papesch, 50 CCPA 1084, 1097, 315 F.2d 381, 391, 137 USPQ 43, 51 (1963)...An element in determining obviousness of a new chemical compound is the motivation of one having ordinary skill in the art to make it. That motivation is not abstract, but practical, and is always related to the properties or uses one skilled in the art would expect the compound to have, if made. In re Stemniski, supra note 10, at 1416-17, 444 F.2d at 585-86, 170 USPQ at 347 (1971)... No common properties presumption rises from the mere occurrence of a claimed compound at an intermediate point in a conventional reaction yielding a specifically named prior art compound. That an intermediate/end-product relationship exists between a claimed compound and a prior art compound does not *alone* create a common-properties presumption...(emphasis added)

201 USPQ at 557-8.

In view of the foregoing, applicants respectfully submit that the claimed compounds are not obvious over the "positional isomers" of Watsuka. Accordingly, applicants request that the rejection of obviousness over Watsuka be withdrawn.

Since all the claims in the application are now in proper form and patentably distinguished over the cited art, an early allowance and notice thereof are courteously requested.

Respectfully submitted,



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